

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

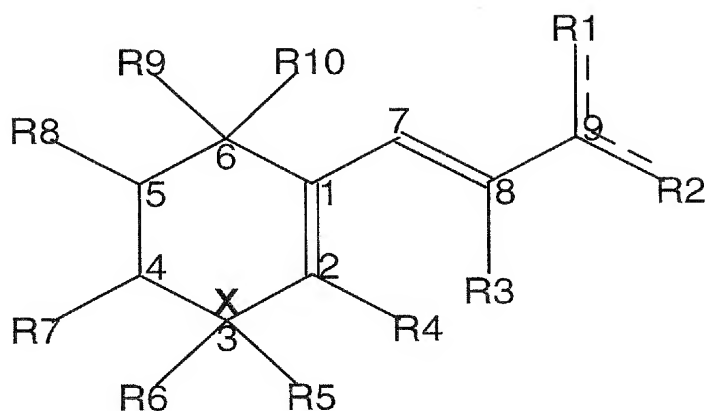
Claims 1 - 58 (Canceled)

59. (New) A method of preventing or treating non-proliferative diabetic retinopathy, in a mammal by administering an effective amount of a medicament comprising at least one compound capable of inhibiting the visual cycle, to said mammal.

60. (New) The method of claim 59, wherein said mammal is a human being.

61. (New) The method of claim 59, wherein said mammal has been diagnosed with diabetes.

62. (New) The method of claim 59, wherein the at least one compound comprises a compound of the formula I:

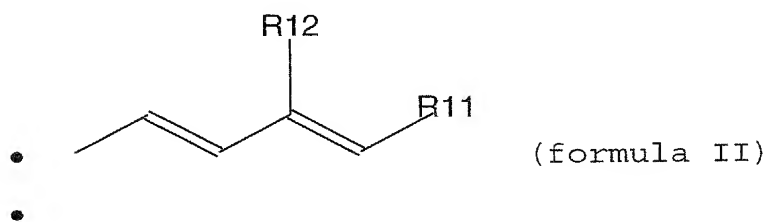


(formula I)

wherein R1 is:

- a lower alkyl, preferably  $\text{CH}_2\text{CH}_3$  or  $\text{CH}_3$ , having a single bond to the carbon at position 9 (C9), wherein the bond between C9 and R2 preferably is a double bond, or
- $\text{CH}_2\text{OH}$  or  $\text{CHO}$  or  $\text{CF}_3$ , or
- $\text{CH}_2$  with a double bond to C9, or
- a bond from C9 to R2, or
- OH

and wherein R2 is:



(formula II)

wherein R11 is selected from the group consisting of:

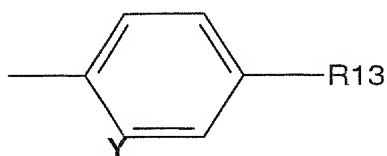
- an alcohol group, such as  $-\text{CH}_2\text{OH}$ ,
- an aldehyde group, such as  $-\text{CHO}$ ,
- carboxy ( $-\text{COOH}$ ),
- a lower alkyl group, such as  $-\text{CH}_3$ ,
- an ether group, such as  $-\text{CH}_2\text{OCH}_3$ ,  $-\text{CH}_2\text{OC}_4\text{H}_9$ ,  $-\text{CH}_2\text{OC}_6\text{H}_5$  or  $-\text{CH}_2\text{OC}_8\text{H}_{17}$ ,

- an ester group, such as  $-\text{CH}_2\text{OCOCH}_3$ ,
- a amine derivative, such as  $-\text{CH}_2\text{NHCOCH}_3$ ,  $-\text{CH}_2\text{NHCOC}_6\text{H}_5$ , or  $-\text{CH}_2\text{NCH}_3\text{COCH}_3$ ,
- $-\text{CH}_3\text{COC}_6\text{H}_5$ ,
- $-\text{CH}=\text{NOH}$ ,
- $-\text{CH}=\text{NNHCOCH}_3$ ,
- $-\text{CH}=\text{C}(\text{COCH}_2\text{CH}_2\text{CH}_3)_2$ ,
- $-\text{CH}=\text{C}(\text{COCH}_2)_2$ ,
- $-\text{CH}=\text{C}(\text{COCH}_2)_2\text{CH}_2\text{CH}=\text{C}(\text{COCH}_2\text{CH}_2)_2\text{CH}_2$ ,
- $-\text{COOCH}_3$ ,
- $-\text{COOCH}_2\text{H}_5$ ,
- $-\text{COZ}$ , wherein Z is an amino acid, such as glycine, leucine, phenylalanine, or tyrosine,
- $-\text{CONHC}_2\text{H}_5$ ,
- $-\text{CONHC}_3\text{H}_7$ ,
- $-\text{CONH}_2\text{C}_2\text{H}_4\text{OH}$ ,
- $-\text{CONH}_2\text{C}_3\text{H}_6\text{OH}$ ,
- $-\text{CONH}_3\text{C}_3\text{H}_6\text{OH}$ ,
- $-\text{CONHC}_6\text{H}_5$ ,
- $-\text{CONH}_2\text{C}_6\text{H}_4\text{OH}$ ,
- $-\text{CONH}_4\text{C}_6\text{H}_4\text{OH}$ ,
- $-\text{CONH}_2\text{C}_6\text{H}_4\text{COOH}$ ,
- $-\text{CONH}_4\text{C}_6\text{H}_4\text{COOH}$ ,
- $-\text{CH}_2\text{OCOCH}_2\text{Br}$ ,
- $-\text{CH}_2\text{OCOCH}_2\text{Cl}$ ,
- $-\text{COOCH}_2\text{CH}_3$ ,
- an N-alkylamide group, such as  $-\text{CONHR}$ , wherein R is an alkyl, preferably 4-hydroxy-phenyl or ethyl,
- $-\text{COOR}$ , wherein R is beta-D-glucuronide,
- an ethyl sulfone group,
- an ethyl ester group, and
- an alkoxycarbonyl group, such as ethoxycarbonyl

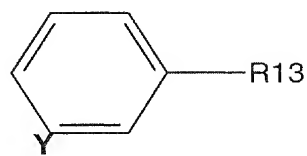
and wherein R12 is:

- a lower alkyl, preferably CH<sub>3</sub> or CH<sub>2</sub>CH<sub>3</sub>, or
- CH<sub>2</sub>OH or CHO or CF<sub>3</sub>,

or R2 is a substituted aryl or heteroaryl, such as:



(formula III) or



(formula IV)

wherein R13 is selected from the group consisting of:

- carboxy (-COOH),
- an alcohol group, such as -CH<sub>2</sub>OH,
- an aldehyde group, such as -CHO,
- CH<sub>2</sub>OCOCH<sub>2</sub>Br,
- CH<sub>2</sub>OCOCH<sub>2</sub>Cl,
- COOCH<sub>2</sub>CH<sub>3</sub>,
- a CONHR group, wherein R is an alkyl, preferably 4-hydroxy-phenyl or ethyl),
- COOR, wherein R is beta-D-glucuronide,
- an ethyl sulfone group,
- an ethyl ester group, and
- an alkoxycarbonyl group, such as ethoxycarbonyl;

and wherein Y is C or N or S or O

or R2 is

- O, having a double bond to C9

wherein R3 is OH or a lower alkyl or H or CH or CHRCH<sub>3</sub>

(wherein R is a double bond to R4),

and wherein R4 is H or CH or OH or a lower alkyl, such as CH<sub>3</sub>,

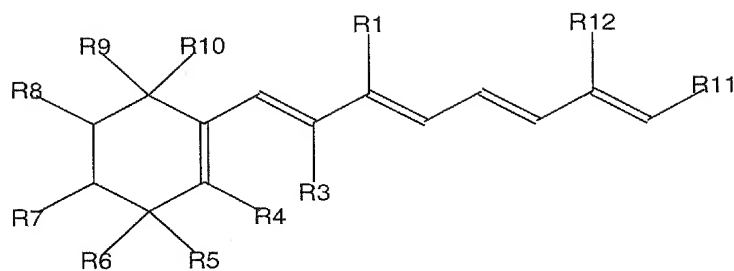
and wherein R5 is OH or a lower alkyl, such as CH3, or H or O (double bond to atom at position 3) or absent,  
and wherein R6 is OH or a lower alkyl, such as CH3, or H or absent or a bond to R5 (if R5 is O) or a bond to C4,  
and wherein R7 is alkoxy, such as methoxy, or OH or a lower alkyl, such as CH3, or H or 3-(1-adamantyl)-4-methoxyphenyl,  
and wherein R8 is OH or a lower alkyl, such as CH3, or H or a bond to C6,  
and wherein R9 is OH or a lower alkyl, such as CH3, or H,  
and wherein R10 is OH or a lower alkyl, such as CH3, or H or a bond to C5,  
and wherein X is C or N or S or O.

and wherein each of R1, R3, R4, R5, R6, R7, R8, R9, R10, R11, R12 and R13, is optionally substituted one or more times with a lower alkyl group, such as a methyl group or an ethyl group,

with the proviso that when R2 is formula II, and R1, R4, R9 and R12 are all CH3, and R3, R5, R6, R7 and R8 are all H and R11 is a carboxy group, the configuration is not 9-cis (2E,4E,6Z,8E) or all-trans,

and the proviso that when R2 is formula II, and R1, R4, R9 and R12 are all CH3, and R3, R5, R6, R7 and R8 are all H and R11 is an alcohol group, the configuration is not all-trans.

63. (New) The method of claim 59, wherein the at least one compound comprises a retinoid, of the formula V:



(formula V)

wherein the configuration of the four isoprenoid units is all trans (E) or one or more is cis (Z).

64. (New) The method of claim 63, wherein the configurations around the carbon-carbon double bands are all-trans (2E,4E,6E,8E) or 9-cis (2E,4E,6Z,8E), or 11-cis (2E,4Z,6E,8E), or 13-cis (2Z,4E,6E,8E).

65. (New) The method of claim 63, wherein R3 is H.

66. (New) The method of claim 63, wherein R4 is CH3.

67. (New) The method of claim 63, wherein R5 is H.

68. (New) The method of claim 63, wherein R6 is H.

69. (New) The method of claim 63, wherein R7 is H.

70. (New) The method of claim 63, wherein R8 is H.

71. (New) The method of claim 63, wherein R9 is CH3.

72. (New) The method of claim 63, wherein R10 is CH3.

73. (New) The method of claim 63, wherein R5 is O and R6 is a bond to R5.

74. (New) The method of claim 63, wherein R3 is H and R4 is CH3, and R5 is O and R6 is a bond to R5, and R7 is H, and R8 is H, and R9 is CH3, and R10 is CH3.

75. (New) The method of claim 63, wherein R3 is H, and R4 is CH3, and R5 is H, and R6 is H, and R7 is methoxy, and R8 is CH3, and R9 is CH3, and R10 is H.

76. (New) The method of claim 63, wherein R11 is selected from the group consisting of:

- COOH,
- an alcohol group, such as -CH2OH,
- an aldehyde group, such as -CHO,
- CH2OCOCH2Br,
- CH2OCOCH2Cl,
- COOCH2CH3,

-CONHR, wherein R is preferably 4-hydroxy-phenyl or ethyl, and

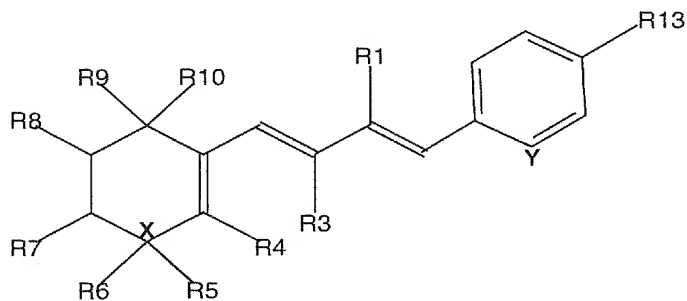
-COOR, wherein R is beta-D-glucuronide.

77. (New) The method of claim 63, wherein R1 is CH3.

78. (New) The method of claim 63, wherein R12 is CH3.

79. (New) The method of claim 59, wherein the at least one compound comprises a compound selected from the group consisting of: isotretinoin (13-*cis*-retinoic acid), 11-*cis*-retinol, 11-*cis*-retinal, 11-*cis*-retinyl bromoacetate, acitretin, etretinate, fenretinide, 4-oxo-isotretinoin, motretinide, retinaldehyde, *all-trans*-retinyl bromoacetate, *all-trans*-retinyl chloroacetate, and retinoyl betagluconide.

80. (New) The method of claim 62, where the compound has the formula VI:

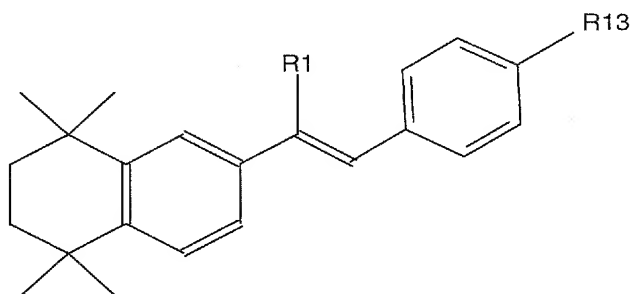


(formula VI)



81. (New) The method of claim 80, wherein R3 and R4 are both CH and are connected by a double bond.

82. (New) The method of claim 81, wherein the compound has the formula VII:



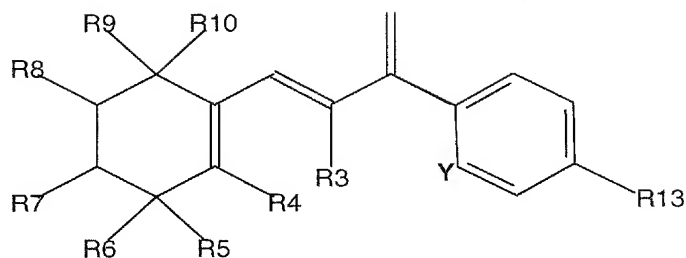
(formula VII)

83. (New) The method of claim 82, wherein R13 is selected from the group consisting of: a carboxy (COOH) group, an ethyl sulfone group, and an ethyl ester group.

84. (New) The method of claim 82, wherein R1 is CH3.

85. (New) The method of claim 59, wherein the at least one compound comprises a compound selected from the group consisting of: arotinoid ethyl ester, arotinoid-free carboxylic acid and arotinoid ethyl sulfone.

86. (New) The method of claim 62, wherein the at least one compound has the formula VIII:



(formula VIII)

87. (New) The method of claim 86, wherein R3 and R4 are both CH and are connected by a double bond.

88. (New) The method of claim 86, wherein R4 is CH and R3 is CHRCH<sub>3</sub>, wherein R is a double bond to R4.

89. (New) The method of claim 86, wherein one or more of R5, R6, R9 and R10 are CH<sub>3</sub>.

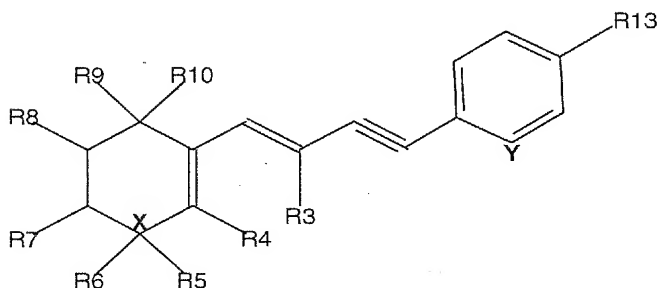
90. (New) The method of claim 86, wherein R7 and R8 are both H.

91. (New) The method of claim 86, wherein Y is C.

92. (New) The method of claim 86, wherein R13 is a carboxy group.

93. (New) The method of claim 59, wherein the at least one compound comprises bexarotene.

94. (New) The method of claim 62, wherein the at least one compound comprises a compound of the formula IX:



(formula IX)

95. (New) The method of claim 94, wherein R3 and R4 are both CH and form a double bond.

96. (New) The method of claim 94, wherein R4 is CH and R3 is CHRCH3, wherein R is a double bond to R4.

97. (New) The method of claim 94, wherein R9 and R10 are both CH3.

98. (New) The method of claim 94, wherein R7 and R8 are both H.

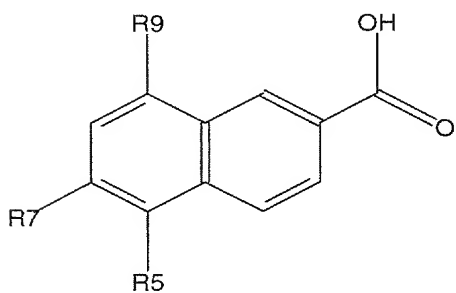
99. (New) The method of claim 94, wherein X is S and R5 and R6 are absent.

100. (New) The method of claim 94, wherein Y is N.

101. (New) The method of claim 94, wherein R13 is a alkoxy carbonyl group, preferably an ethoxy carbonyl group.

102. (New) The method of claim 59, wherein the at least one compound comprises tazarotene.

103. (New) The method of claim 62, wherein the at least one compound comprises a compound of the formula X:



(formula X)

104. (New) The method of claim 103, wherein R5 is H and R9 is H.

105. (New) The method of claim 103, wherein R7 is 3-(1-adamantyl)-4-methoxyphenyl.

106. (New) The method of claim 59, wherein the at least one compound comprises adapalene.

107. (New) The method of claim 59, wherein the at least one compound is DAPP.

108. (New) The method of claim 59, wherein the at least one compound is composed as a pro-drug.

109. (New) The method of claim 59, wherein the medicament is in a form for being administered locally.

110. (New) The method of claim 109, wherein the medicament is in a form for being administered intravitreally.

111. (New) The method of claim 59, wherein the medicament is in device formulation held confined by mechanical or physico-chemical effects.

112. (New) The method of claim 59, wherein the medicament is in a slow-release formulation.

113. (New) A method comprising a pharmaceutical composition suitable for intravitreal implantation comprising a pharmaceutically effective amount of at least one compound capable of inhibiting the visual cycle and/or dark adaptation.

114. (New) The method of claim 113, wherein said pharmaceutically effective amount of said at least one compound is determined by measuring the level of reduction of dark adaptation in a treated subject.

115. (New) The method of claim 113, wherein said pharmaceutical composition is in device formulation held confined by physico-chemical effects.